

**Department of Health and Human Services
National Institute of Environmental Health Sciences
National Cancer Institute**

**Minutes of the Interagency Breast Cancer and Environmental Research Coordinating
Committee Meeting**

September 30-October 1, 2010

The Interagency Breast Cancer and Environmental Research Coordinating Committee was convened for its inaugural meeting on September 30, 2010 at 8:30 a.m. at the J.W. Marriott, 1331 Pennsylvania Avenue, NW, Washington, D.C. The Chair of the Committee had not been determined prior to the meeting.

The meeting was open to the public on September 30, 2010 from 8:30 a.m. to 5:00 p.m. and on October 1, 2010 from 8:30 a.m. to 3:30 p.m. The agenda on September 30, 2010 included a 45 minute session for the purpose of public comment. Notice of the meeting was published in the *Federal Register*.

Members Present

Christine Ambrosone, PhD
Janice Barlow
Beverly Canin
Alice Chang, PhD
Sally Darney, PhD
Suzanne Fenton, PhD
Michele Forman, PhD
Michael Gould, PhD
Sandra Haslam, PhD
Ronda Henry-Tillman, MD, FACS
Karen Joy Miller
Laura Nikolaides, MS
Vivian Pinn, MD
Kenneth Portier, PhD
Jeanne Rizzo, RN
Gayle Vaday, PhD

Ex Officio Members Present

Dale Sandler, PhD
Neeraja Sathyamoorthy, PhD

NIH Staff Present

Linda Birnbaum, PhD, DABT
Gwen Collman, PhD
Robert Croyle, PhD

Gary Ellison, PhD, MPH
Mary Gant
Rachel Gross, MPA
Nonye Harvey, MPH
Christie Kaefer, MBA, RD
Elizabeth Maull, PhD
Sheila Newton, PhD
Britt Reid, DDS, PhD
Les Reinlib, PhD
Deborah Winn, PhD

Institute of Medicine, National Academies of Science

Jane Durch, MA
Lois Joellenbeck, DrPH

Centers for Disease Control & Prevention

Mary White, ScD, MPH

Other

Paolo Boffetta, MD, MPH
Maria Hegstad
Kelly Horton

I. BACKGROUND

The Breast Cancer and Environmental Research Act¹ was signed into law by the President on October 8, 2008, as an amendment to the Public Health Service Act in order to establish a committee on breast cancer and the environment; the committee is tasked with reviewing research conducted or supported by Federal agencies on environmental exposures and breast cancer and making recommendations for innovative research strategies moving forward. The composition of the Presidential advisory committee is to consist of Federal representatives, scientists, health professionals, and people who represent individuals with breast cancer. The Secretary of the U.S. Department of Health and Human Services (HHS), Kathleen Sebelius, delegated the authority for implementing this act in June 2009 to the National Institutes of Health (NIH), and the Director of the NIH delegated the task specifically to the National Institute of Environmental Health Sciences (NIEHS) and the National Cancer Institute (NCI) in July 2009.

The duties of the committee, as set forth in the authorizing legislation, are to:

* This meeting summary was prepared with Federal funds from the National Cancer Institute, National Institutes of Health (contract number HHSN261200900025I). The statements, conclusions, and recommendations contained in this document reflect opinions of the meeting participants and are not necessarily intended to represent the official position of any Federal agency, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

¹ Text of the Act is available from <http://www.govtrack.us/congress/billtext.xpd?bill=h110-1157>.

- Share and coordinate information on existing research activities and make recommendations to the NIH and other Federal agencies regarding how to improve existing research programs that are related to breast cancer research;
- Develop a comprehensive strategy and advise the NIH and other Federal agencies in the solicitation of proposals for collaborative, multidisciplinary research, including proposals to evaluate environmental and genomic factors that may be related to the etiology of breast cancer that would:
 - Result in innovative approaches to study emerging scientific opportunities or eliminate knowledge gaps in research to improve the research portfolio;
 - Outline key research questions, methodologies, and knowledge gaps;
 - Expand the number of research proposals that involve collaboration between two or more national research institutes or national centers, including proposals for Common Fund research, to improve the research portfolio; and
 - Expand the number of collaborative, multidisciplinary, and multi-institutional research grants;
- Develop a summary of advances in breast cancer research supported or conducted by Federal agencies relevant to the diagnosis, prevention, and treatment of cancer and other diseases and disorders;
- Make recommendations to the Secretary of HHS:
 - Regarding any appropriate changes to research activities including recommendations to improve the research portfolio of the NIH;
 - To ensure that the activities of the NIH and other Federal agencies are not duplicative;
 - Regarding public participation in decisions relating to breast cancer research to increase the involvement of patient advocacy and community organizations;
 - On how to best disseminate information on breast cancer research progress; and
 - On how to expand partnerships between public entities, including Federal agencies, and private entities to expand collaborative, cross-cutting research.

The timeline for the creation of the Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC) has been as follows:

- September 2009—Charter filed
- October 2009—*Federal Register* announcement requesting nominations of committee members
- January/February 2010—Committee selection and beginning of vetting process
- August 2010—Press release announcing the committee

The IBCERCC held its first meeting, hosted by the NIEHS and the NCI, in Washington, DC, on September 30-October 1, 2010. Attendees of the meeting included committee members, presenters, and invited participants representing multiple Federal agencies, independent scientists and doctors, and members of the community. The meeting agenda included an overview of the IBCERCC's charge as set forth in the authorizing legislation, presentations covering the relevant research activities of several Federal agencies, and general committee discussion about logistics, committee leadership, and plans for the committee's final report.

II. Welcome and Charge to the Committee

History and Legislative Overview

Linda S. Birnbaum, PhD, DABT, ATS, Director, NIEHS and National Toxicology Program

There has been a gradual rise in the incidence of breast cancer between 1975 and 2000 among White and African American women despite decades of research on the causes of breast cancer. During the early 1990s breast cancer advocacy organizations brought to the attention of the NIH and Congress that everyday exposures in our environment, such as chemicals acting as estrogens in the human body, may contribute to the high incidence of breast cancer seen in some communities. These advocates wanted scientists to be open to the possibility that breast cancer is not only a genetic or hormonal disease, but also may be caused by a variety of environmental exposures.

Mortality rates overall have declined over the same time period due to improved detection and treatment options. However, younger women with breast cancer tend to have more aggressive and harder to treat subtypes. The lifetime risk of being diagnosed with breast cancer is now one in eight. The probability of developing breast cancer increases with age.

Many breast cancer risk factors that have been established by researchers as being associated with a strong increase in risk are immutable, such as age, being female, family history of breast cancer, and specific genes.² Factors associated with a moderate increase in risk are related to endogenous estrogens, other physiologic characteristics, or hormone replacement therapy. Some of the risk factors associated with a weak increase in risk are also difficult to consciously modify like age at menarche or menopause, although through new research we know that exposure to some environmental chemicals may impact puberty and age at menopause. Other weak risk factors are alterable such as alcohol consumption. Research is inconclusive at this point about environmental causes, which make some of which make sense biologically and toxicologically and tend to be of great interest to the public. More research is needed on environmental causes.

The 2008-2009 Annual Report of the President's Cancer Panel³ titled *Reducing Environmental Cancer Risk: What We Can Do Now*⁴ may provide a framework for thinking about this committee's task. The report calls for increased attention to the overall impact of hazardous exposure on cancer risk and the lack of public awareness. Advocacy groups have been calling for increased awareness and action on breast cancer and environmental causes. Explaining the increase in breast cancer incidence over time will require attention to the interaction of environmental factors.

The charge to the IBCERCC is to address the legislative mandate boldly and provocatively, consider the totality of issues and prioritize them, and develop a usable product that will guide the future of federally conducted and supported research on breast cancer and the environment.

² The presentation included information on specific risk factors identified by the American Cancer Society, available from <http://www.cancer.org/Cancer/BreastCancer/DetailedGuide/breast-cancer-risk-factors>.

³ Panel information is available from <http://deainfo.nci.nih.gov/advisory/pcp/index.htm>.

⁴ Full report is available from http://deainfo.nci.nih.gov/advisory/pcp/annualReports/pcp08-09rpt/PCP_Report_08-09_508.pdf.

Challenges and Opportunities for Studying Physical and Chemical Environmental Exposures and Breast Cancer

Robert T. Croyle, PhD, Director, Division of Cancer Control and Population Sciences, NCI

A Federal advisory committee lends visible credence to a cause. This committee functions in part as a public voice for holding the NIH accountable for progress and for synthesizing research evidence and disseminating it in a way that communities and the public can understand, which is critical considering the many complexities and unknowns.

The study of environmental exposures and breast cancer is challenging due in part to complex methodological issues. Reasons for this complexity include: a) breast cancer susceptibility varies over the course of the lifespan; b) individual susceptibility varies based on genetics and the interaction of specific genetic factors and mixtures of a variety of environmental exposures; c) breast cancer is clinically and molecularly heterogeneous and the etiology of these subtypes may be different; this is particularly challenging because it can be complicated to communicate to the public about different “kinds” or subtypes of breast cancer.

There also are challenges associated with studying specific physical and chemical exposures. The exposures experienced by the general population tend to be low level and ubiquitous, and may change over time. Bisphenol A (BPA) is an example of a ubiquitous chemical present in consumer products such as drinking bottles, food can liners, water pipes, and dental sealants. The rise in exposures to ionizing radiation from medical diagnostic imaging tests is an example of an exposure that has become more common over time. These exposures may occur in a variety of settings, including the home and worksite, and many may be pervasive features of the environment that make assessment complicated. Assessment technology is rapidly developing and changing, which provides opportunities scientifically, but increases the complexity of what defines a “good” environmental breast cancer study. The exposure may precede cancer development by decades, yet participants in traditional cohort studies often are not recruited until they are adults. Newer cohort studies, such as the National Children’s Study, will try to assess environmental exposures early in the life span, but are not designed to examine breast cancer. Relying on self-report is insufficient because people may be unaware of exposures or do not remember. Exposure effects may result from mixtures of chemicals, rather than single elements, and some chemicals stored in body tissues are not accessible to researchers (e.g., fat tissue).

Advances in understanding breast cancer and possible environmental causes will depend on collaboration across organizations, new assessment technologies, the use of natural experiments (e.g., exposure to new pollutants in China), the interaction between genetics and the environment, and providing information about risk to communities in more effective ways. Dissemination efforts must address the public’s distrust of scientific evidence and attitudes about government; information sharing should be consumer-friendly and user-centered.

III. Committee Logistics

Deborah M. Winn, PhD, Deputy Director, Division of Cancer Control and Population Sciences, NCI

The members of the committee have been nominated, selected, and vetted in accordance with the Breast Cancer and Environmental Research Act and the guidelines of the Federal Advisory Committee Act of 1972 (FACA)⁵ to include scientists, physicians, and other health professionals; members of the general public who represent persons with breast cancer; voting Federal members; and non-voting Federal members. The executive secretaries for the committee are Drs. Gwen Collman and Deborah Winn. Their duties are to work closely with the committee and committee chair(s) to accomplish the goals of the committee and develop the final report. They will oversee any NIH staff and contracts related to the committee's work and will ensure that timelines are met. Support from other NIEHS and NCI extramural staff will include working with the subcommittees, assisting with writing, problem solving with the executive secretaries, and other operational tasks.

The primary responsibility of the committee is to prepare a report, in accordance with the duties set forth in the authorizing legislation, to the Secretary of HHS. The IBCERCC may elect to produce additional reports if deemed appropriate. The committee members need to elect a chair or co-chairs, contribute to discussions, help define the scope of the report, identify information and resources needed in order to prepare the report, write the report, and address comments on the draft in preparation of the final report. There is flexibility in how the committee moves forward in terms of scheduling face-to-face meetings, teleconferences, and webinars, and designing committee and subcommittee structure. The chair or co-chairs will work closely with the executive secretaries. A tentative timeline includes completing a draft report by October 2011, conducting peer review and Federal agency clearance activities in October-December 2011, revising the report in January/February 2012, and submitting a final report to the Secretary by March 2012. It is hoped that the Secretary will respond to the final report with instructions to Federal agencies for action in accordance with the recommendations

Discussion

The committee discussed the overlap of the IBCERCC's work and that of the Institute of Medicine (IOM) committee funded by Susan G. Komen for the Cure titled Breast Cancer and the Environment: The Scientific Evidence, Research Methodology, and Future Directions.⁶ Dr. Lois Joellenbeck and Jane Durch, study directors for the IOM committee and invited participants of the IBCERCC meeting, briefly explained the mission of the IOM committee. The IOM committee is not specifically charged with reviewing the portfolio of research supported or conducted by Federal agencies. Both committees are tasked with identifying research gaps. The IOM committee will examine methodological issues and provide research recommendations as well as consider potential actions that women could take to reduce their risk of breast cancer; it will produce a technical report and a summary for the lay audience by August 2011.

IV. Overviews of Research Related to Breast Cancer and the Environment: Reports from Federal Members

National Institute of Environmental Health Sciences

⁵ Information on the FACA rules is available from <http://www.gsa.gov/portal/category/21242>.

⁶ Information about the IOM committee is available from <http://www.iom.edu/Activities/Environment/BreastCancerEnvironment.aspx>.

Gwen W. Collman, PhD, Interim Director, Division of Extramural Research and Training, NIEHS

The NIEHS supports investigator-initiated research from basic biology to population studies; develops scientific research initiatives that expedite research in understudied areas; and conducts intramural programs in the areas of physical and chemical causes of cancer in general, as well as breast cancer specifically. The NIEHS is responsible for the National Toxicology Program (NTP), which has identified more than 50 industrial and environmental chemicals as breast carcinogens. Between 1985 and 1995 NIEHS researchers discovered that there were health effects of chemicals that mimic estrogens starting with diethylstilbestrol (DES), a chemical used in the 1950's to prevent pregnancy complications, which formed the basis for future work. Estrogen receptors as targets for xenoestrogens is a major focus. An NIEHS team discovered the BRCA1 gene in 1994 and continues that work today. The NIEHS collaborated with the NCI on the Northeast Mid-Atlantic and Long Island Breast Cancer studies. The process of the Long Island study helped formulate and substantiate the value of including advocates in the research process.

NIEHS research between 1996 and 2010 includes work on a class of chemicals that are endocrine disruptors; early windows of exposure; fetal basis of adult disease; a shift of thinking about mammary gland biology; and how to use animal models to look at difference exposures. The NIEHS is the lead agency on a Roadmap project on epigenetics, the study of inherited changes in phenotype or gene expression caused by mechanisms other than changes in the underlying DNA sequence and acquired changes due to factors such as environmental exposures. The Sister Study is also being conducted as part of the Intramural program at NIEHS, studying over 50,000 sisters of women with breast cancer to better understand the role of the environmental and genetic causes of the disease.

The majority of breast cancer and environment research awards funded by the NIEHS have focused on examining the impact of specific exposures on breast cancer risk. The number of publications from NIEHS-funded extramural research on breast cancer and environment has increased from approximately 15 in 1994 to close to 80 in 2009. Papers are being published in more high-quality journals today and are helping to stimulate debate. The NIEHS also funds programs to encourage graduate and post-doctoral students to build a career in this area.

The presentation included highlights from an NIEHS brainstorming workshop in 2002; Breast Cancer and Environment Research Centers (BCERC) projects; Division of Extramural Research and Training (DERT) projects; and Division of Intramural Research (DIR) projects including the Sister Study and discovery of the BRCA1 gene.

The goals of the BCERC include developing new data, conducting a longitudinal study of environmental and genetic factors of puberty, and integrating results to disseminate public health messages. The key elements for success include shared governance of this work—involving advocates in research development and implementation and collaborating between basic science programs of animal research and public health research (epidemiology studies). BCERC includes three areas: epidemiology, basic biology, and Community Outreach and Translation Cores (COTCs). Breast cancer advocates have been very active in the COTCs and the BCERC as a

whole. Examples include their service on the project steering committee, a public education video about the need for animal research produced and disseminated by Zero Breast Cancer, and opportunities for advocates to spend time in Center laboratories to better understand the concepts of contemporary research.

Future directions for the NIEHS include continuing studies on early environmental exposures and puberty and other windows of susceptibility to environmental influences, the transition from centers to a research network, continued work on biomarkers and biosensors of exposure, and following children's cohorts, such as the National Children's Study.

Discussion

Discussion centered on the measure of success for a research program. Advocates and representatives of clinical medicine stressed the importance of research impacting incidence of breast cancer and actual changes in a person's life, and not simply the number of publications produced. For example, many insurance companies still will not pay for a woman to be tested for the BRCA1 gene that was discovered by NIEHS researchers in 1994. Other measures of success that do not depend on seeing immediate shifts in incidence rates or mortality are also necessary because an intervention can have a profound effect but may not be apparent until years later due to latency and other competing risk factors. There needs to be a way to translate research findings into practical application for real people. There has been improvement since involvement of breast cancer advocates in the research process, and these are the very issues on which the IBCERCC should deliberate and provide recommendations on how to be more effective. Publications are important in that they are for other scientists and groups to build upon; consistency in findings across many studies is required before a particular finding can be reliably reported to the public.

National Toxicology Program (NTP)

Suzanne E. Fenton, PhD, Reproductive Endocrinologist, NTP

The intent of the NTP vision is to expand the scientific basis for making public health decisions on the potential toxicity of environmental agents. The NTP engages in four primary functions: chemical testing, public health reporting, technical development of novel methods (e.g., new animal models and high throughput), and training and leading (e.g., workshops and post-doc trainees).

The NTP has contributed to the field of research on breast cancer and the environment. The Congressionally mandated 11th annual *Report on Carcinogens*⁷ identified 246 carcinogens known or reasonably anticipated to be hazardous. The 12th edition is due out in December 2010. NTP studies on mammary cancer have included 2-year rat and mouse studies of 555 substances with varying effects on mammary gland tumors. A 2006 NTP workshop⁸ on human relevance of hormonally induced reproductive tumors resulted in recommendations for studies with extended

⁷ Available from <http://ntp.niehs.nih.gov/index.cfm?objectid=72016262-BDB7-CEBA-FA60E922B18C2540>.

⁸ Thayer KA, Foster PM, 2007 Workgroup Report: National Toxicology Program Workshop on Hormonally Induced Reproductive Tumors—Relevance of Rodent Bioassays. *Environ Health Perspect* 115(9): doi:10.1289/ehp.10135

exposures (*in utero* and during puberty) rather than just adult virgin mice and rats and the evaluation of mammary gland whole mounts (i.e. the entire mammary gland is placed on a slide for microscopic examination). Specific rat and mouse strains were identified as being susceptible or resistant and therefore better or worse suited for studies on hormonal mammary carcinogens. Specific exposure periods across the life cycle were identified as critical periods for mammary gland development: gestational/neonatal, peripubertal, and pregnancy. Studies in conjunction with the NCTR have determined that a longitudinal section of tissue prepared for pathological assessment is superior to the transverse section in screening for mammary gland cancers because it incorporates the entire gland and will assist in detection of inflammation, hyperplasia, structural changes, and small tumors. Differences between mouse models and human disease still exist, some of which may never be resolved.

Discussion

Discussion included the caution that chemicals need to be examined in conjunction with time of exposure; some chemicals may slow growth of tumors in adults, but actually spur growth in developmental periods. A study on the Seveso cohort found a dose-related increase in breast cancer among those exposed to dioxin when they were younger.⁹ This has implications for future research because developmental exposures have not been included in past 2 year bioassays.

Discussion also centered on what may be the most sensitive endpoint. Although the mammary gland has been found to be the most sensitive biological target in several studies, it is possible that the mammary gland may not be the best endpoint to examine in all cases; development of the gland and other endpoints should be evaluated in tandem following early life environmental exposures.

Advocates raised the question of how findings of carcinogens in animal models can be translated to humans. One example of researchers trying to address this issue is a commentary included in the meeting materials by Brody et al. (2007) that reviewed recent epidemiological research to examine how the field has addressed issues raised by animal studies.¹⁰

National Cancer Institute

Britt C. Reid, DDS, PhD, Chief, Modifiable Risk Factors Branch, Epidemiology and Genetics, NCI

The NCI approaches its mission through intramural research (approximately 15 percent of budget in FY09) and extramural (approximately 80 percent of budget in FY09) research, training, and partnerships. Several projects represent partnerships with other institutes, particularly the NIEHS. Intramural research projects include a study titled “Breast Cancer and the Environment” which focuses on women with cancer susceptibility genes looking at exposures that differentially affect risk; the Polish Breast Cancer Study focusing on tobacco,

⁹ Multiple publications resulted from studies of the Seveso, Italy cohort. One example involving dose-response is available from <http://www.ncbi.nlm.nih.gov/pubmed/10739069>.

¹⁰ Brody JG, Rudel, RA, Michels, KB et al. Environmental pollutants, diet, physical activity, body size, and breast cancer: Where do we stand in research to identify opportunities for prevention? *Cancer*. 2007; 109: 2627-2634. <http://onlinelibrary.wiley.com/doi/10.1002/cncr.22656/pdf>. Accessed October 13, 2010.

hormone, and chemical exposures; the Cancer in Women study of 75,000 women in Shanghai, China, focusing on occupational exposures; and, the Agricultural Health Study of 90,000 subjects looking at numerous environmental exposures in partnership with the NIEHS, the National Institute for Occupational Safety and Health (NIOSH) at the Centers for Disease Control and Prevention (CDC), and the Environmental Protection Agency (EPA). The NCI intramural program averaged about 45 projects at approximately \$35 million per year from FY07 through FY09.

Funding for extramural research on breast cancer and the environment has increased steadily since 1994 until a peak in 2003 with a concomitant rise in relevant publications. Publications are just one way to measure the productivity of grantees. Extramural grants addressing breast cancer and the environment have focused primarily on the effects of tobacco, radiation, and lifestyle factors; some have also addressed pesticides, polychlorinated biphenyl (PCB), dioxins, general chemicals, phenols or BPA, and the social environment. Training grants account for 10 percent of projects funded.

Highlights of recent findings include the association between smoking and estrogen receptive breast cancer in young women; the association between cumulative second-hand smoke exposure and increased postmenopausal breast cancer among non-smokers; the association between folate intake and reduced estrogen receptor breast cancer risk; and separate associations of physical activity and soy food intake with reduced risk for premenopausal breast cancer.

In the future, the NCI would like to expand the use of current infrastructures and mechanisms, such as the exposure biology program of the Genes, Environment and Health Initiative, and the cohort consortium, which brings together 41 large high-quality cancer epidemiology cohorts world-wide to collaborate, share, and standardize protocols and data collection. Using these infrastructures and applying a windows of susceptibility and life-course approach will help us to better understand environmental exposures and breast cancer risk.

Discussion

Discussion centered on the availability of reviewers and scientific peer-review groups that are appropriate for creative research in the areas of toxicology and environmental exposure. A major concern is that standing study sections currently do not incorporate this type of expertise. The organization of study sections is slow to change. One way to address the issue is through the Center for Scientific Review (CSR), which organizes the NIH study sections that evaluate 70 percent of the research grant applications sent to the NIH, but this can be slow. Another approach is to ask for a special review by reviewers who are identified as meeting the specific needs of applications. The executive secretaries or staff can provide information on the expertise represented on the standing study sections if the committee would find that helpful.

Department of Defense (DOD)

Gayle G. Vaday, PhD, Program Manager, Breast Cancer Research Program, Congressionally Directed Medical Research Programs, DOD

The Breast Cancer Research Program (BCRP) is part of the Congressionally Directed Medical Research Program (CDMRP) at the Department of Defense (DOD) and is located within the Army Medical Command at Fort Detrick. The CDMRP had a history of biomedical research and development when Congress appropriated money for the BCRP to it in 1993; at that time it did not have experience as a grant funding agency. The CDMRP commissioned the IOM to advise on a management strategy and review system. Other research programs have been added over the years including ovarian and prostate cancers. The BCRP uses a broad definition of environment.

The BCRP funds innovative high-risk/high-gain investigator-initiated research that might not be considered by other agencies; opportunities to produce preliminary data for further funding; interdisciplinary research teams including scientists and advocates; multi-team awards; and training for future innovators. Breast cancer and environment awards account for 7.6 percent of the total awards given, with the majority going to innovation-based awards.

Examples of awards include those investigating exposure to cadmium, air pollutants, and environmental factors stemming from the Long Island Breast Cancer Study, endocrine-disrupting chemicals, the role of gut microflora, environmental factors affecting racial/ethnic disparities, and *in utero* exposures. The BCRP does not use standing study sections, but rather recruits reviewers based on proposals received; they utilize a two-tiered review system with both scientific and programmatic reviews.

Centers for Disease Control and Prevention (CDC)

Mary White, ScD, MPH, Chief, Epidemiology and Applied Research Branch, Division of Cancer Prevention and Control, CDC

Activities at the CDC related to breast cancer and the environment occur in three centers: the National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP), the National Center for Environmental Health (NCEH), and NIOSH. Three ways in which the CDC seeks to accomplish its mission and address breast cancer and the environment are by monitoring health, detecting and investigating health problems, and conducting research to enhance prevention. The CDC does not typically fund extramural research, but sometimes Congress will provide funds through earmarks.

The CDC administers the National Program of Cancer Registries, which currently covers the entire U.S. population by combining Federal and state cancer registries. Data on approximately 200,000 new invasive breast cancer cases are submitted to the CDC each year. National cancer statistics are available to the public online and can be examined by geographical area, subtypes of breast cancer, race/ethnicity, and other variables.¹¹ A lay person can use the database to map the incidence of breast cancer in his or her state. Another way the CDC works to monitor health is by taking the lead on developing capabilities to measure low levels of chemicals.¹²

One area of CDC interest has been the breast cancer rate among Native Alaskan women, which led to the linking of records from the Indian Health Services for surveillance. The NCEH has been looking at persistent environmental agents in Alaska, where the rates of breast cancer are

¹¹ United States Cancer Statistics are available from <http://apps.ncccd.cdc.gov/uscs/>.

¹² Exposure report is available from www.cdc.gov/exposurereport.

highest. The Marin Women's study investigated a high rate of breast cancer in Marin County, California.

NIOSH staff is most involved in etiologic research. For example, one study looked at the cancer experience of Pan Am flight attendants, which was unique in terms of collecting reproductive and family histories as well as occupational exposures. The CDC's Division of Laboratory Sciences (DLS), NCEH, and external researchers have collaborated on various studies. Other examples of relevant research at the CDC include the Women's Contraceptive and Reproductive Experiences Study (CARE) and the Human Genome Epidemiology Navigator (HuGE).

Future directions for the CDC include comparative effectiveness research, incorporating occupational information in cancer registry, addressing health education for breast cancer awareness in young women, and as part of the Hormone Standardization Project improving detection of individuals at risk for breast cancer and other diseases by standardizing how chemicals are examined across studies.

Discussion

The National Conversation on Public Health and Chemical Exposures¹³ led by the Agency for Toxic Substances and Disease Registry (ATSDR) at the CDC was discussed as a potential resource that can inform this committee's work. The National Conversation process brought multiple constituencies together to write a report on education and communication, policies and practices, health disparities, and other topics. Others noted that this could be informative, but was not specifically about breast cancer.

Environmental Protection Agency (EPA)

Sally P. Darney, PhD, Acting National Program Director, Human Health Research Program, Office of Research and Development, US Environmental Protection Agency

Although the EPA does not have a research program that focuses specifically on breast cancer, it does participate in collaborative programs with the NIEHS, FDA and NIH designed to reveal pathways through which chemicals can induce toxicity, including carcinogenesis. The EPA also partners with the CDC, NIEHS, and NIH on the National Children's Study funded through the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The EPA's Office of Research and Development (ORD) spends approximately \$20M per year on extramural grants in the area of human health, including those focused on children's exposures and health and evaluating the impact of exposures in community and home settings. While the EPA's primary responsibility is regulatory and its actions are dictated by legislation, ORD is leading an effort to advance the field of toxicology beyond regulatory requirements by applying a systems approach to chemical testing and risk assessment, including an increased understanding of environmental factors related to cancer risk.

EPA is developing an integrated chemicals program called Safer Products for a Sustainable World. The goal of this program is to create a new paradigm for assessing thousands of manmade and natural products. Research will also address the complexity of exposures in

¹³ Information on the National Conversation is available from <http://www.atsdr.cdc.gov/nationalconversation/>.

community settings. Multiple chemicals may be present in the environment in proportions that vary by geography and place (e.g., indoor versus outdoor). Community-based research considers chemical stressors along with natural stressors. For example, research is evaluating the distribution of allergens and pollen, and how, as a system, such stressors may exacerbate asthma.

The Safer Products for a Sustainable World Program will look first at the inherent properties of chemicals that make them toxic, an approach that can be adapted for high throughput screening. Some of these properties are related to cancer. The goal is to use this preliminary process to decide which chemicals should be given the highest priority for further study using in vitro screens and strategic in vivo approaches.

Once toxicity is established, the likelihood of human exposure becomes an important consideration when ranking chemicals for further strategic testing whether for cancer and/or non-cancer effects. In real world scenarios the risk of chemical exposures and their effects also need to be considered with respect to other factors that determine health before decision makers can determine which solutions will have the greatest impact. Geographic information system (GIS) models can also be used to link data at larger scales such as air and water pollution at the ecosystem level, and integrate it with public health tracking data such as that assembled by CDC in order to evaluate the relationship between chemical exposures and public health.

The EPA has recently created a publically accessible database called the Toxicity Reference Database (ToxRefDB)¹⁴ that includes information from 3,200 studies on more than 500 chemicals. A preliminary analysis of this database identified thirty-seven chemicals exhibiting mammary gland effects characterized by a number of different pathologies. This sort of analysis can be used to identify chemicals for further, more detailed evaluation as potential carcinogens.

Risks of environmental chemicals, including risks for breast cancer, are determined by many factors including: biological susceptibility factors (such as age, gender, developmental stage, and pre-existing disease), exposure vulnerability factors (such as smoking and proximity to pollution sources), and social/behavioral factors (such as cultural practices). Also, disproportionate risk factors such as socio-economic status (SES), lack of social capital, and access to health have been shown to influence a person's response to environmental contaminants.

In summary, EPA's research on chemicals, integrated with the many factors that impact susceptibility and vulnerability to chemically-induced health effects, provides the scientific foundation for understanding environmental contributions to breast cancer and other human disease.

Office of Research on Women's Health (ORWH), NIH

Vivian W. Pinn, MD, Director, Office of Research on Women's Health, NIH

The Office of Research on Women's Health (ORWH) was established in 1990 within the Office of the Director of the NIH. The ORWH funds or co-funds research with and through the ICs; determines research priorities in collaboration with the ICs; coordinates activities related to women's health and sex differences; and provides reports for Congress and the advocacy

¹⁴ Available from <http://actor.epa.gov/toxrefdb>.

community on progress in women's health research. The ORWH was originally created because of a concern that women were not included in clinical studies and came about because of grassroots efforts.

Most NIH research on breast cancer and environment is funded through the NCI and NIEHS; however, 69 active grants related to this topic are funded across 17 other ICs. Several of these are not specifically about breast cancer, but are related to it (e.g., health impact of endocrine disruptors in the border area and effects of ethanol exposure during the regression of mammary tissue to a non-secreting state on post-partum breast cancer). Examples of research funded or co-funded by the ORWH include dietary lignin effects on hormone, growth and signaling factors in breast tumors (with the NCI), and exploratory studies on the anti-breast cancer function of bamboo extract with the National Center for Complementary and Alternative Medicine.

The ORWH holds an annual Women's Health Seminar Series open to the public, and this year the focus is Environmental Exposures and Women's Health. It is trying to disseminate the series to the broader community.¹⁵

The ORWH recently released its new strategic plan, *Moving into the Future with New Dimensions and Strategies: A Vision for 2020 for Women's Health Research*, which included three volumes: executive summary;¹⁶ regional scientific working group reports; and public testimony. The executive summary prioritizes all the recommendations yielded from the process into six goals. Two of the goals relate to the mission of the IBCERCC: create strategic alliances and partnerships to maximize the domestic and global impact of women's health research and develop and implement new communication and social networking technologies to increase understanding and appreciation of women's health and wellness research.

The Environment and Women's Health working group made several recommendations as part of the strategic plan process. These recommendations were: understand the effects of chemical exposures on disease etiology in women; expand the capacity of assessment technology; pioneer research efforts to identify and eliminate negative effects of environmental factors; partner with communities to better translate and disseminate evidence to improve clinical care, policy, and community health; and, develop partnerships that include interdisciplinary approaches and community participation.

The goal of research should be to impact women's health by implementing findings into clinical practice and communicating effectively with policy makers. Challenges of research translation and implementation include communicating effectively about different types of research (e.g., health policy, basic, or applied); getting information incorporated into community behaviors and health care providers' practices; better synthesizing complex information; and deciding as a scientific community when and how to publicize and disseminate research results and how to explain inconsistent findings.

Discussion

¹⁵ The archived video of the last session in the series on October 5, 2010, is available from <http://videocast.nih.gov/summary.asp?Live=9691>.

¹⁶ Volume 1 is available from http://orwh.od.nih.gov/ORWH_Strategic-Plan_Vol_1_508.pdf.

There was brief discussion on the overlap of focus on gender differences at the ORWH and the work of the IBCERCC. For example, the gender of the offspring in preeclamptic women has an effect on the mother's subsequent risk of breast cancer, indicating the route of exposure to fetus or from pregnancy back to the mother. Among the goals the IBCERCC has discussed thus far, gender differences may deserve to be highlighted more.

V. Overview of International Research on Environmental Factors and Breast Cancer

Paolo Boffetta, MD, MPH, Deputy Director, Tisch Cancer Institute, Mount Sinai School of Medicine

The incidence of breast cancer is now equal in high-income countries and low- to middle-income countries; this is a new trend because breast cancer used to be a disease of industrialized nations. China and India have almost as many breast cancer cases as the United States. There are 458,000 breast cancer deaths worldwide each year: 189,000 deaths in high-income countries and 269,000 in low-income countries. However, there is a large gap between high- and low-income countries in breast cancer mortality rates. China and India have lower incidence rates but higher rates of breast cancer mortality than the United States and European Union (EU). Reliable data, where available in individual countries, show that breast cancer incidence has been increasing steadily since the 1960s. Possible explanations for the trend are changes in reproductive history (e.g., younger age at menarche, fewer pregnancies, older age at first pregnancy, lower rate and shorter duration of breastfeeding), changes in nutrition and lifestyle (e.g., higher body-mass index, lower physical activity, higher caloric intake), and environmental exposures.

Analysis of data from surveys of women provides an idea of the extent to which particular changes can explain the increase in breast cancer incidence. For example, the reduction of the number of children born to women in Brazil between 1980 to 2006 accounts for an 18.9 percent change in breast cancer rates. Another example is based on a 1992 survey in urban China that indicates 8 percent of the change in the breast cancer rate can be attributed to overweight and obesity.

The European Commission (EC) provides funding for international research throughout the EU.¹⁷ The goal of the EC's research program is to avoid replicating research funded at the national level and to promote multi-institution, multi-country projects mainly through requests for proposals. There is a trade-off between the goal of coordinating existing research projects and funding for original, innovative research. The Community Research and Development Information Service for Science, Research, and Development (CORDIS)¹⁸ is the official source of information for calls for proposals through the Seventh Framework Programme (FP7). The goals of CORDIS include facilitating participation in European research activities; enhancing exploitation of research results; and promoting dissemination.

There are not as many EC research projects on breast cancer and environment as there are funded by the NIH. EC research projects on breast cancer and environmental exposures include large-

¹⁷ More information on EC research is available from <http://ec.europa.eu/research/index.cfm?lg=en>.

¹⁸ More information on CORDIS is available from http://cordis.europa.eu/home_en.html.

scale integrated projects, medium-scale projects, small-scale projects, networks, and fellowships. The Collaborative Oncological Gene-environment Study (COGS) is a large-scale 5-year project involving 16 partners aimed at identifying individuals with increased risk of breast, ovarian, and prostate cancers through identifying gene-environment interactions in a dataset of 200,000 individuals. Genomics Biomarkers of Environmental Health is a 5-year medium-sized study with 11 partners looking at the association of biomarkers predictive of increased risk for several diseases and environmental exposures. Reproductive Effects of Environmental Chemicals in Females (REEF) is a 5-year small-scale project involving six partners investigating the reproductive effects of long-term exposure of endocrine disrupting compounds at low environmental concentrations using animal models.

Other international cancer research funding agencies include the World Cancer Research Fund International ¹⁹ and the Association for International Cancer Research.²⁰

Research on environmental exposures and breast cancer is mainly funded at the national level. There is a need for better coordination of research efforts world-wide. There is an overlap between breast cancer and environment research and research on the reproductive effects of endocrine disruptors and breast cancer genetics. Many opportunities exist for research among populations in transition.

Discussion

The committee discussion focused on several topics related to international research. There has been no direct impact of the June 2007 EU regulation on the safe use of chemicals, Registration, Evaluation, Authorisation, and Restriction of Chemical Substances (REACH), on the EC research program to date.

The impact of EC research on public policy is unclear. The EC research program is young and works through a different framework of priorities every 5 years and each framework overlaps with the terms of EC members. Changes in funding schemes make it difficult to track results over time. The EC produces booklets within each funding program showing what has been funded and the main results, but the impact that this dissemination of results has had on public policy is unclear.

Worldwide epidemiology trends may provide clues about environment, diet, and pollution effects on different types of breast cancer. For example, premenopausal breast cancer rates are similar worldwide, but postmenopausal breast cancer rates are much higher in the United States than in other countries. Most international data are not specific to pre- and postmenopausal women, but age can be considered a proxy. There is not currently much international research being conducted specifically on premenopausal breast cancer.

The incidence of breast cancer in selected international populations increased at a higher rate starting in the late 1970s or early 1980s. It may be important to place that trend within the historical context at the time. That is also about the time when health disparities started

¹⁹ More information on the World Cancer Research Fund International is available from <http://www.wcrf.org/>.

²⁰ More information on the Association for International Cancer Research is available from <http://www.aicr.org.uk/>.

appearing and when the standard of care for breast cancer changed from mastectomy to lumpectomy. Perhaps an examination of what was happening in public health, medical care, or broader policy at the time could yield information about the trends. It is also possible that the time frame of the increase is not the time frame we need to look at, considering the uptick could be the result of environmental exposures decades earlier.

There are many opportunities for research on environmental exposures in international settings due to naturally occurring events such as contaminated ground water in Bangladesh and populations changes accompanying industrialization in the Philippines and China.

VI. Specific Topic Discussions and Areas of Critical Scientific Importance

1. Defining Environment

Discussant: Sheila Newton, PhD, Director, Office of Policy, Planning and Evaluation, NIEHS

The definition of “environment” differs depending on a person’s perspective (e.g., scientist, sociologist, lay person). This committee will need to define the scope of the term “environment” for the purposes of the report. Some examples of what could be included in the environment in terms of breast cancer are hazardous chemicals, household agents, pesticides, endocrine disruptors, lifestyle factors, stress, and health care disparities.

Discussion

In terms of breast cancer, one definition of environment could simply include that which is *not* genetics. The legislative history of the authorizing legislation for the IBCERCC included a focus on physical and chemical environmental exposures, but it may be important to include other aspects of environment as well such as lifestyle factors. Another intention of the law was to focus on promoting research that will enable action to impact breast cancer prevention, incidence, and mortality. Aspects of the definition that could be included are intermittent versus continuous exposures, gene-environment interactions, and mixtures of environmental exposures. Also it will be important to include other factors that alter a person’s susceptibility to develop breast cancer associated with an environmental exposure.

It was suggested that the committee define environment broadly and then focus on particular aspects that will be feasible to address for the purposes of the report. It is challenging to incorporate multiple dimensions of environment (e.g., built environment, social environment, medical environment, geographic environment) as well as types of environmental exposures (e.g., physical and chemical, lifestyle and social) while also addressing the relevant relationships (e.g., gene-environment interaction, exposure mixtures, dosing and timing of exposures). An overarching conceptual framework of the environment may be more helpful than a definition listing individual exposure items.

2. Overview of Current Understanding of Breast Cancer and Environment

Discussants: Suzanne E. Fenton, PhD, Reproductive Endocrinologist, NTP and Jeanne Rizzo, RN, President and CEO, Breast Cancer Fund

Breast cancer is a global problem; 1.5 million women will be diagnosed in 2010. Research has shown that between 10 to 27 percent of the variance in breast cancer rates can be explained by genetics, leaving the larger portion accounted for by environment and lifestyle. Breast cancer risk is extremely complex. The interactions and relationships between windows of susceptibility, gene-environment interactions, and exposure to environmental mixtures are very important to the overall understanding.

Animal models have not traditionally focused on the mammary gland as a sensitive target tissue, and there are a limited number of studies that have focused on multiple endpoints including the mammary gland, or looked at timing and dose range of effects. Few chemical testing programs routinely require mammary glands as mandatory tissues to be examined; currently the NTP requires it, but other agencies may not. More data on chemical effects in developmentally exposed mammary tissue, especially when compared to other reproductive tissue outcomes, are needed.

The real life issues of timing of exposures, low-dose exposures, which do not follow linear dose-response curves, mixtures, and interactions will all be important in understanding breast cancer risk. We need a clear understanding of critical periods and windows of susceptibility in women through longitudinal studies. Animal models can be used to address specific targets, lifestyle issues (e.g., diet, health and beauty aid use, etc.), ethnic disparities (comparison of sensitive strains), and the role of precocious breast development in breast cancer risk. More understanding is needed about how data from animal studies can be translated to humans.

Discussion

Examining exposures and factors at the time of diagnosis and in earlier life periods should not be an either/or discussion; both are important to understanding breast cancer risk. Another aspect to understand is how environmental exposures may differentially impact the subtype and the aggressiveness of the breast cancer rather than just overall breast cancer risk. Possible protective environmental and lifestyle factors, such as lactation, should also be further examined.

The California Breast Cancer Research Program (CBCRP) has funded an initiative that will use mathematical and infectious disease modeling to design an interactive website where the user can click on a particular risk factor and it will display the strength of evidence shown by research using International Agency for Research on Cancer (IARC) methodology and literature references that support each risk factor. It will allow the user to eliminate a particular risk factor from the model and see how it changes the predictability of risk.²¹ The project should be done by the end of this year.

3. Insights from the Study of Normal Mammary Gland Development

Discussants: Sandra Z. Haslam, PhD, Director, Breast Cancer and the Environment Research Center, Michigan State University and Michael N. Gould, PhD, Professor of Oncology, University of Wisconsin at Madison

²¹ More information about the California Breast Cancer Research Program initiative is available from http://www.cbcpr.org/research/PageGrant.asp?grant_id=6450.

The study of normal mammary gland biology has yielded insights for breast cancer risk. Environmental exposures can: a) mimic, increase, or inhibit hormones or growth factors; b) target regulatory functions of connective tissue; and, c) alter gene expression patterns and signaling pathways. The specific outcome in these three cases is highly dependent on the mammary gland stage of development (e.g., *in utero*, puberty, post-pregnancy). Effects of environmental exposure are also highly dependent on differences in genetic background; genetic manipulation in animal models provides opportunities to look at gene-environment interactions and how to apply this information to human heterogeneity.

The study of carcinogenesis has yielded insights for breast cancer risk. There are many differences between humans and animals. Development of *in vivo* humanized models has been useful; putting a human immune system and human mammary gland in a rodent may lead to better models. Epigenetics needs to be a future approach. We should be able to extrapolate back from the Cancer Genome Anatomy Project (CGap) and The Cancer Genome Atlas Project (TCGA). Population risk for breast cancer assigned by inherited genetics or environmental exposure does not say anything about individual risk. We need to combine an individual's genetics, environmental exposures, physiology, and window of susceptibility in order to better estimate individual risk. We need to use a systems biology approach to relate risk to complex genetics, complex environment (e.g., low-dose mixtures), and specific windows. A major challenge is how to translate this type of research to risk assessment and breast cancer prevention in humans, and this challenge should be addressed through a systems approach.

Discussion

One area that is understudied is the role of intergenerational effects; animal researchers can assess what type of intergenerational effects mark subsequent generations for the onset of puberty.

The utility of cell lines in high-throughput testing was discussed as an alternative method. Not every environmental exposure will affect the target cell. If one only looks at the target cell, some things may be missed; the exposure could modify the stroma or milieu instead. It also is important to be very specific about the question to be answered with cell lines. Another issue is knowing what cells to culture. Some alleles that influence risk of breast cancer will act in epithelial cells, while some act in specific T-cells. Highly complex screening can be used to determine this, but it is difficult.

These humanized models are hypothetical so the utility for breast cancer is unknown at this point.

4. Windows of Susceptibility to Environmental Agents

Discussants: Sally P. Darney, PhD, Acting National Program Director, Human Health Research Program, EPA and Michele R. Forman, PhD, Professor of Epidemiology, The University of Texas, MD Anderson Cancer Center

The life-course schemata includes periconceptual, *in utero*, infancy, childhood, adolescence, perimenopausal, and postmenopausal. Endogenous exposures include hormones, growth factors,

physical activity, and diet. Exogenous exposures include pharmaceuticals, chemicals, and other environmental exposures. Exposures occur across the life course and influence breast cancer risk and can occur intermittently or chronically during various windows of susceptibility. We do not fully understand intra-individual variation within each window of susceptibility. For example, there is tremendous variation in rate of growth among infants. There are complex issues to consider within each window of susceptibility including intermittent versus chronic exposure, cumulative body burden, dosage and route of exposure, risk to mother and offspring, extrapolation from animal research, gene-environment exposures, and epigenetic effects from exposures.

The majority of epidemiological research in cancer has focused on adulthood. More recently the focus has shifted to the fetal period. A study of the relationship between preeclampsia in pregnant women and breast cancer risk was presented as an example. The cohort was followed from *in utero* through 13 years of age. Girls born to mothers without preeclampsia (normotensive) have increased odds of early breast development if their greatest weight gain occurred between 3 and 6 months of age. Girls born to mothers with preeclampsia have increased odds of early breast development if their greatest weight gain occurred between 6 and 12 months of age. Another study showed a relationship between the timing of greatest infancy weight gain and risk of menarche prior to 12 years of age.

Discussion

There is a dearth of information particularly for the first pregnancy and perimenopausal periods during the life course; these may represent unique opportunities for research. Finding animal models that mimic specific windows of susceptibility is difficult. For example, middle-aged female rats do not have a perimenopausal period that correlates with humans; rather they experience a constant estrous phase. We need to examine what is occurring during lactation and why it might be protective. It could be that lack of ovulation during lactation reduces lifetime exposure to hormones.

Examining specific subtypes of breast cancer and the role of risk during particular windows of susceptibility is very complex. For example, early pregnancy can be protective, but not for all kinds of breast cancer. Early pregnancy may increase risk for triple negative breast cancer, but only among certain populations. Most studies lack enough statistical power to analyze subtypes, and animal models do not always reproduce the same subtypes seen in humans.

5. Characterizing and Testing for Environmental Exposures

Discussants: Ronda S. Henry-Tillman, MD, Medical Director, Women's Oncology Clinic; Director, Cancer Control at the Arkansas Cancer Research Center, University of Arkansas for Medical Sciences and Gayle Vaday, PhD, Program Manager, BCRP, CDMRP, DOD

We cannot currently characterize and assess a breast cancer patient's individual environmental exposure in order to prevent breast cancer in family members. Human population factors for chemical testing include the timing of exposure, susceptibility, and socioeconomic factors. The Breast Cancer and Chemicals Policy Project²² funded by CBCRP will identify biological

²² Information is available from <http://coeh.berkeley.edu/greenchemistry/cbcrp.htm>.

processes associated with breast cancer and toxicity testing assays for evaluating chemicals as well as design and pilot an overall Hazard Identification Approach. Remaining questions include: a) how can we study the causes of breast cancer with more precision; and b) how can we improve our ability to measure the range of environmental exposures? Working across disciplines is going to be important for moving forward in this field.

Discussion

Each Federal agency has a different approach to funding and soliciting research. There is an opportunity to look across all agencies and identify the gaps and possibilities for increased synergy. The DOD approach to research and development is product driven, which is a very different model than that of the NIH. Perhaps there are some product goals for exposure assessment technology.

The Department of Energy may be a resource for the committee because it has experience studying Hiroshima and Nagasaki in collaboration with the National Academy of Sciences (NAS); it has many resources and datasets.²³ Although radiation is an example for which exposure and dosing can be quantified, a sample from one point in time may not reflect exposures over time. There might be opportunity with animal studies to conduct research that will increase understanding about dosing and dose rate. Most federally funded research in this area is not investigator-initiated.

In a clinical setting most breast cancer patients provide samples for biobanking. There appear to be many biospecimen resources and data that could help with understanding environmental factors. Perhaps once animal work is completed, researchers could refer to a database of all current and past longitudinal studies to identify what specimens have been collected during what time period. For example, if an animal study reveals that the infant period is important for a particular exposure, then a person could look to the database to see if there are relevant human specimens available to investigate. Maybe there is a way to be more strategic about mining the animal data so that investments can be targeted and prioritized in subsequent human studies so as to maximize the chance of finding effects and minimizing sample waste.

6. Translation and Community Participation

Discussants: Janice Barlow, Executive Director, Zero Breast Cancer and Christine Ambrosone, PhD, Professor of Oncology, Roswell Park Cancer Institute in Buffalo, NY and Member, Board of Scientific Advisors, NCI

There are multiple definitions for “research translation.” Research is of little value unless there is utility to it and an impact on outcomes related to decision makers and consumers. The final endpoint from a community perspective is reducing breast cancer incidence and mortality, reducing environmental exposures, and building a healthier environment.

²³ Other examples were suggested as models for future research involving collaboration among multiple disciplines that resulted in the pooling of resources, reduction of duplication, and building on others’ knowledge, e.g., the Black Sea Ecosystem Recovery Project (BSERP).

Research translation raises multiple challenges: a) creating effective messages that integrate findings from different types of research; b) prioritizing messages for the public; c) identifying appropriate channels of dissemination for particular audiences; d) translating findings into utility for the public; e) evaluating the impact of dissemination on endpoints; and f) integrating research findings into health care practice and prevention.

Community participation in the research process is based on the belief that those who are affected by a decision have a right to be involved in the decision making process. Participation involves two-way communication and collaborative problem solving and enhances a community's ability to address its own health needs while ensuring researchers understand community priorities. Some models of public participation in the research process include the National Conversation on Public Health and Chemical Exposures, California Environmental Contaminant Biomonitoring Program, CBCRP Special Initiatives, and Boston Consensus Conference on Human Biomonitoring. Community-engaged research describes a continuum of possibilities for research conducted with a community partner and represents a process of conducting research, not a method.

There are approximately 600 breast cancer organizations across the United States; some of them do not consider the environment. There may be an opportunity to educate these organizations.

Community participation in the research process raises multiple challenges: a) determining the most efficient ways to elicit public participation; b) ensuring equality among partners; c) maximizing the benefits for community organizations to participate; d) determining an appropriate model; e) making research data available to the public; f) evaluating community engagement; and g) ensuring that the community understands the research in which they it is involved.

Discussion

The discussion covered various aspects of research translation and dissemination. Research findings are inherently complex, and it can be difficult to communicate the nuances to the lay public. Some editors see the role of their publications as primarily to inform “other researchers” rather than as a source of conclusive findings that will impact directly on public behavior, clinical practice, or policy. It is difficult to ensure that the public understands this and does not get confused or frustrated by tentative or mixed findings. However, no one should act as a “gatekeeper” in restricting publications from being available to the public. Publicly funded research is catalogued on PubMed and is available to the public. The complexity of research is not a reason to withhold new findings.

There may be models that exist for “grading” the strength of evidence from particular studies so as to communicate simply to the lay reader how to interpret findings in the larger context of literature. Creating these models involves a great deal of work and a large expense, and many only deal with a handful of topics or elements because it is difficult to reach a consensus on the strength of each assertion. It would be very complex for a topic such as breast cancer and environmental exposures, but still may be a framework or strategy to consider moving forward.

Part of research translation to the public needs to involve identifying the strength, value, and context for particular research findings.

The role of the media and other methods for dissemination of research were discussed. The media can sometimes obscure the research translation to the public by reducing interviews with researchers to sound bites that, when taken out of context, may be confusing or contradictory. Other methods, such as posting web videos of entire speeches to substantiate quotes taken out of context, social networking media, and posting information on websites, are ways to ensure that the whole message is shared.

There is a difference between disseminating research findings as they are published and using a body of research evidence to craft specific public health messages. Translating research based on specific audiences may be useful; for example, an advocacy organization will need different types of information than the general public. There are many purposes of research translation that should be considered: for the general knowledge of the public, to inform advocacy organizations in order to respond to their constituencies, to communicate to decision makers, and to inform policy makers.

There is a value to engaging community participation early in the research process because it also assists with the dissemination of the research by creating a built-in constituency that can help get the message out.

VII. General Discussion to Define Scope of the IBCERCC Report

The committee collaboratively drafted an outline during the meeting for the IBCERCC report to serve as a starting point for identifying the end product. Discussion surrounding the creation and revision of this draft document evolved around several themes.

The final report needs to incorporate a definition of environment that starts with the big picture and then narrows the body of the report into specific sub-topics. The final report should be driven by the language in the authorizing legislation, incorporate overarching themes and values, and include specific goals for specific agencies. Even though there is overlap with the IBCERCC work and that of others, there are two unique aspects to the committee's approach: a) the IBCERCC is specifically charged with focusing on identifying research gaps and strategies across all Federal agencies and b) the IBCERCC can look at this topic across the life course, including normal and abnormal, and through the lens of community participation.

One goal of the report will be to have an impact on the research process. The goal is innovative research on environmental exposures and breast cancer that will advance understanding, fill research gaps, and have an impact on incidence and mortality. The IBCERCC's product needs to be a strategy for how collaborative, interdisciplinary research that achieves this aim will be fostered and solicited. This strategy may incorporate existing mechanisms (e.g., Common Fund), borrow mechanisms from different agencies (e.g., DOD model), or create new mechanisms for innovation and collaboration across disciplines and agencies. Having a framework of normal and abnormal development will help identify the gaps in research.

Discussion of the draft outline revealed an equal emphasis on three components of the report: a) the state of the science and conceptualization of the scientific themes; b) the process, how agencies will work to achieve goals, how collaboration will occur to achieve scientific agenda; and c) translation and dissemination.

The committee discussed ways in which the public could inform the creation of the report. One method members generally agreed upon is to publish a request for information in the *Federal Register* with a short set of specific questions. The responses may not be large in number, but they tend to be in-depth and of high quality. In addition, public comments are welcome during official committee meetings or by submitting written comments to the committee.

VIII. General Discussion on Committee Organization

The executive secretaries led a discussion on committee organization. The group determined that it will elect three equal co-chairs²⁴, none of whom will be Federal employees: one basic scientist, one epidemiologist or clinician, and one person representing the advocacy community. Members nominated themselves or others to be considered as co-chairs. An email ballot will be distributed to the members at a later date for voting.

The co-chairs will work closely with the executive secretaries to set meeting agendas, determine priorities and needs of the committee, define the work scope, and organize subcommittees and their responsibilities.

IX. Timeline

1. Research and identify gaps—first six months
2. Develop recommendations and strategic plan
3. Mid-2012 product finalized

X. Adjournment

The meeting was adjourned at 3:30 on October 1, 2010.

CERTIFICATION

/Michele Forman/

Michele Forman, PhD

Chairperson

Interagency Breast Cancer & Environmental Research Coordinating Committee

/Gwen W. Collman/

Gwen W. Collman, PhD

Executive Secretary

Research Process Subcommittee

²⁴ Following the meeting, it was determined that the Committee was not permitted to elect more than one overall Chair as per the Charter.

Interagency Breast Cancer & Environmental Research Coordinating Committee

Proper signatures

Treat as signed, § 1.4(d)(2)